ENT COOPERATION TREA

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 21 December 1999 (21.12.99)	
International application No. PCT/GB99/01441	**Applicant's or agent's file reference** SMK/CP5775069
International filing date (day/month/year) 07 May 1999 (07.05.99)	**Priority date** (day/month/year) 08 May 1998 (08.05.98)
Applicant ARMOUR, Kathryn, Lesley et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

02 December 1999 (02.12.99)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer S. Mafla
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

3023501

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
SMK/CP5775069		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB99/01441	07/05/1999	08/05/1998
International Patent Classification (IPC) or national classification and IPC		
C07K16/00		
Applicant		
CAMBRIDGE UNIVERSITY TECHNICAL SERVICES..et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
02/12/1999	30.05.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Hinchliffe, P Telephone No. +49 89 2399 8431

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT - SEPARATE SHEET

International application No. PCT/GB99/01441

ITEM V

1. In addition to the documents cited in the search report three other documents pertaining to the same field have come to light. These are as follows:
D5a US-A-5 834 597, D5b Cole et al, J.of Immunol. 1997, vol.159, 3613-3621,
D6 Mueller et al, Mol. Immunol. 1987, vol.34(6), 441-452.

   In all the documents cited the functional requirement of binding to either FcRn or Fc RIIb with the particular changes made within the immunoglobulin regions are not shown. Consequently the claims fulfill the requirements of Article 33(2) PCT. In addition the retention of the bindings with the changes made were not derivable in an obvious way from the documents cited and consequently the requirement of Article 33(3) is also fulfilled.

2. For the assessment of the present claims 23-29 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

ITEM VII

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents cited are not mentioned in the description, nor are these documents identified therein.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01441

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-31
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-31
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-22,30,31
	No:	Claims	23-29(?)

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01441

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-55 as originally filed

Claims, No.:

1-31 as received on 16/05/2000 with letter of 16/05/2000

Drawings, sheets:

1/14-14/14 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

Article 34

Claims

1. A binding molecule which is a recombinant polypeptide comprising:
(i) a binding domain capable of binding a target molecule, and
(ii) an effector domain having an amino acid sequence substantially homologous to all or part of a constant domain of a human immunoglobulin heavy chain;
wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target,
characterised in that the effector domain is
- capable of specifically binding FcRn and/or FcγRIIb, and
- a chimeric effector domain which is derived from two or more human immunoglobulin heavy chain C_H2 domains including a first human immunoglobulin heavy chain C_H2 domain wherein 2, 3 or 4 amino acids in at least 1 region of the C_H2 domain have been modified to the corresponding amino acids from a second, different, human immunoglobulin heavy chain C_H2 domain,

wherein the region is selected from the 2 discrete regions numbered residues 233-236, and 327-331 in accordance with the EU numbering system,

and wherein in each case the human immunoglobulin is selected from IgG1, IgG2 and IgG4.

2. A binding molecule as claimed in claim 1 wherein the first human immunoglobulin is selected IgG1, IgG2, and IgG4, and the second human immunoglobulin is selected from IgG2 and IgG4.

A 3. A binding molecule as claimed in claim 1 ~~or claim 2~~ wherein 2 amino acids in 1 region of the C_H2 domain are modified to the corresponding amino acids from a second human immunoglobulin heavy chain C_H2 domain.

A 4. A binding molecule as claimed in claim 1 ~~any one of the preceding claims~~ wherein at least 2 amino acids in each of the 2 discrete regions of the C_H2 domain are modified to the corresponding amino acids in the corresponding region in a second and third human immunoglobulin heavy chain C_H2 domain respectively.

A 5. A binding molecule as claimed in claim 1 ~~any one of the preceding claims~~ wherein the effector domain shares at least

about 90% sequence identity with the first human immunoglobulin heavy chain C_H2 domain.

A 6. A binding molecule as claimed in ~~any one of the preceding claims~~ Claim 1 comprising a human immunoglobulin heavy chain C_H2 domain having one or more of the following amino acids or deletions at the stated positions in accordance with the EU numbering system:

Posn	Amino acid
233	P
234	V
235	A
236	(No residue) or G
327	G
330	S
331	S

A 7. A binding molecule as claimed in ~~any one of the preceding claims~~ Claim 1 comprising a human immunoglobulin heavy chain C_H2 domain having one or more of the following blocks of amino acids or deletions at the stated positions in accordance with the EU numbering system: 233P, 234V, 235A and no residue at 236; or 233P, 234V, 235A and 236G; and/or 327G, 330S and 331S.

A 8. A binding molecule as claimed in ~~any one of claims 5 to 7~~ Claim 5 wherein the effector domain is selected from G1Δab, G2Δa or G1Δac.

A 9. A binding molecule as claimed in ~~any one of the preceding claims~~ Claim 1 further comprising modifications to render the molecule substantially null allotypic.

A 10. A binding molecule as claimed in ~~any one of the preceding claims~~ Claim 1 wherein the effector domain has a reduced affinity for FcγRI, FcγRIIa or FcγRIII and a reduced ability to mediate complement lysis by comparison with the first or second human immunoglobulin heavy chain C_H2 domain.

11. A binding molecule as claimed in claim 10 wherein the effector domain has retained an affinity for FcγRIIb.

A 12. A binding molecule as claimed in ~~any one of the preceding claims~~ Claim 1 wherein the binding domain derives from a different source to the effector domain.

13. A binding molecule as claimed in ~~any one of the preceding claims~~ Claim 1 wherein the binding domain is selected from the binding site of an antibody; an enzyme; a hormone; a receptor; a cytokine or an antigen; a ligand or an adhesion molecule.

14. A binding molecule as claimed in ~~any one of the preceding claims~~ Claim 1 wherein the binding domain is capable of binding any of; the RhD antigen of red blood cells; an HPA alloantigen of platelets; a neutrophil antigen; a T-cell receptor; integrin; GBM collagen; Der P1; HPA-1a; VAP-1; laminin; lutheran; platelet glycoprotein VI; platelet glycoprotein Ia/IIa.

15. A binding molecule as claimed in claim 14 wherein the binding domain is selected from that of CAMPATH-1 and FOG1; OKT3; B2 (anti-HPA-1a); VAP-1; murine anti-α3 (IV) NC1; YTH12.5 (CD3); 2C7 (anti-Der p I); anti-laminin; anti-lutheran.

16. An isolated nucleic acid comprising a nucleotide sequence encoding the effector domain of the binding molecule as claimed ~~in any one of the preceding claims~~ Claim 1.

17. A nucleic acid as claimed in claim 16 wherein the nucleotide sequence encodes a binding molecule as claimed in ~~any one of the preceding claims~~ Claim 1.

18. A nucleic acid as claimed in claim 16 ~~or claim 17~~ which is a replicable vector.

19. A nucleic acid as claimed in claim 18 wherein the nucleotide sequence is operably linked to a promoter.

20. A host cell comprising or transformed with the vector of claim 19 ~~or claim 20~~.

21. A process for producing a binding molecule as claimed in ~~any one of claim 1 to 15~~ Claim 1, the process comprising the step of modifying a nucleotide sequence encoding a first human immunoglobulin heavy chain C_H2 such that 2, 3 or 4 amino acids in at least 1 region of the C_H2 domain corresponds to an amino acid from a second human immunoglobulin heavy chain C_H2 domain,

wherein the region is selected from the 2 discrete regions

numbered residues 233-236, and 327-331 in accordance with the EU numbering system,

and wherein in each case the human immunoglobulin is selected from IgG1, IgG2 and IgG4.

22. A process as claimed in claim 21 wherein 2 amino acids in 1 region of the C_H2 domain are modified to the corresponding amino acids from a second human immunoglobulin heavy chain C_H2 domain.

A 23. Use of a binding molecule or nucleic acid as claimed in ~~any one of claims 1 to 19~~ Claim 1 to bind a target molecule with said binding molecule.

24. Use as claimed in claim 23 wherein the target molecule is FcγRIIb, which binding causes inhibition of one or more of: B cell activation; mast cell degranulation; phagocytosis.

25. Use as claimed in claim 24 to prevent, inhibit, or otherwise interfere with the binding of a second binding molecule to the target molecule.

26. Use as claimed in claim 25 wherein the second binding molecule is an antibody.

A 27. Use as claimed in claim 25 ~~or claim 26~~ wherein the target molecule is selected from: the RhD antigen of red blood cells; an HPA alloantigen of platelets; a neutrophil antigen; a T-cell receptor; integrin; GBM collagen; Der P1; HPA-1a; VAP-1; laminin; lutheran; platelet glycoprotein VI; platelet glycoprotein Ia/IIa.

35A 28. Use as claimed in ~~any one of claims 24 to 27~~ Claim 24 for the treatment of a patient for a disorder selected from: Graft-vs-host disease; host-vs-graft disease; organ transplant rejection; bone-marrow transplant rejection; autoimmunity such as vasculitis, autoimmune haemolytic anaemia, autoimmune thrombocytopenia and arthritis; alloimmunity such as foetal/neonatal alloimmune thrombocytopenia; asthma and allergy; chronic or acute inflammatory diseases such as Chrohn's; HDN; Goodpastures, sickle cell anaemia, coronary artery occlusion.

A 29. Use as claimed ~~any one of claims 23 to 28~~ Claim 23 wherein the binding molecule is administered to a patient, or optionally

in cases where the patient is an unborn infant, to the mother of the patient.

30. A pharmaceutical preparation comprising a binding molecule as claimed in ~~one of claims 1 to 15~~ claim 1, or a nucleic acid as claimed in ~~any one of claims 17 to 19~~ claim 17, plus a pharmaceutically acceptable carrier.

31. An oligonucleotide selected from:

MO22BACK: 5' TCT CCA ACA AAG GCC TCC CGT CCT CCA TCG AGA AAA 3'

MO22: 5' TTT TCT CGA TGG AGG ACG GGA GGC CTT TGT TGG AGA 3'

MO7BACK: 5' TCC TCA GCA CCT CCA GTC GCG GGG GGA CCG TCA GTC 3'

MO21: 5' GAC TGA CGG TCC CGC GAC TGG AGG TGC TGA GGA 3'

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

KREMER, Simon M.
MEWBURN ELLIS
York House
23 Kingsway
London WC2B 6HP
GRANDE BRETAGNE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	30.05.2000
Applicant's or agent's file reference: SMK/CP5775069	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB99/01441	07/05/1999	08/05/1998

Applicant: CAMBRIDGE UNIVERSITY TECHNICAL SERVICES..et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Borinski, W Tel.+49 89 2399-8237

Form PCT/IPEA/416 (July 1992)

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C07K 16/00, 19/00, C12N 15/12, 15/62, C07K 16/34, A61K 47/48, C07K 16/28, C12N 15/13, 15/63, 5/10, A61K 39/395

A1

(11) International Publication Number: WO 99/58572

(43) International Publication Date: 18 November 1999 (18.11.99)

(21) International Application Number: PCT/GB99/01441

(22) International Filing Date: 7 May 1999 (07.05.99)

(30) Priority Data:
9809951.8 8 May 1998 (08.05.98) GB

(71) Applicant *(for all designated States except US)*: CAMBRIDGE UNIVERSITY TECHNICAL SERVICES LIMITED [GB/GB]; 20 Trumpington Street, Cambridge CB2 1QA (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: ARMOUR, Kathryn, Lesley [GB/GB]; 43 High Street, West Wratting, Cambridge CB1 5LU (GB). CLARK, Michael, Ronald [GB/GB]; 124 Richmond Road, Cambridge CB4 3PT (GB). WILLIAMSON, Lorna, McLeod [GB/GB]; 157 High Street, Harston, Cambridge CB2 5QD (GB).

(74) Agents: KREMER, Simon, M. et al.; Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP (GB).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: BINDING MOLECULES DERIVED FROM IMMUNOGLOBULINS WHICH DO NOT TRIGGER COMPLEMENT MEDIATED LYSIS

(57) Abstract

Disclosed are binding molecules which are recombinant polypeptides comprising: (i) a binding domain capable of binding a target molecule, and (ii) an effector domain having an amino acid sequence substantially homologous to all or part of a constant domain of a human immunoglobulin heavy chain; characterised in that the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and more preferably wherein the effector domain is capable of specifically binding FcRn and/or FcγRIIb. These are generally based on chimeric domains which are derived from two or more human immunoglobulin heavy chain C_H2 domains. In preferred embodiments the regions 233–236, and 327–331, are modified, as are further residues to render the molecule null allotypic. The binding domain may derive from any source appropriate to the (usually clinical) application for the molecule and may be from e.g. an antibody; an enzyme; a hormone; a receptor; a cytokine or an antigen; a ligand and an adhesion molecule. Also disclosed are nucleic acids, host cells, production processes and materials, and uses e.g. to inhibit B cell activation; mast cell degranulation; phagocytosis, or to inhibit the binding of a second binding molecule to the target molecule. Pharmaceutical preparations are also disclosed.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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PATENT COOPERATION TREATY

PCT

REC'D 02 JUN 2000

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
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PCT/GB99/01441	07/05/1999	08/05/1998
International Patent Classification (IPC) or national classification and IPC C07K16/00		
Applicant CAMBRIDGE UNIVERSITY TECHNICAL SERVICES..et al.		

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   - VII ☒ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
02/12/1999	30.05.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Hinchliffe, P Telephone No. +49 89 2399 8431

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01441

I. Basis of the report

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1-55	as originally filed			

Claims, No.:

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1/14-14/14	as originally filed

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4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-31
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-31
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-22,30,31
	No:	Claims	23-29(?)

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

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1. In addition to the documents cited in the search report three other documents pertaining to the same field have come to light. These are as follows:
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D6 Mueller et al, Mol. Immunol. 1987, vol.34(6), 441-452.

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ITEM VII

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents cited are not mentioned in the description, nor are these documents identified therein.

Claims

1. A binding molecule which is a recombinant polypeptide comprising:
(i) a binding domain capable of binding a target molecule, and
(ii) an effector domain having an amino acid sequence substantially homologous to all or part of a constant domain of a human immunoglobulin heavy chain;
wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target,
characterised in that the effector domain is
- capable of specifically binding FcRn and/or FcγRIIb, and
- a chimeric effector domain which is derived from two or more human immunoglobulin heavy chain C_H2 domains including a first human immunoglobulin heavy chain C_H2 domain wherein 2, 3 or 4 amino acids in at least 1 region of the C_H2 domain have been modified to the corresponding amino acids from a second, different, human immunoglobulin heavy chain C_H2 domain,

wherein the region is selected from the 2 discrete regions numbered residues 233-236, and 327-331 in accordance with the EU numbering system,

and wherein in each case the human immunoglobulin is selected from IgG1, IgG2 and IgG4.

2. A binding molecule as claimed in claim 1 wherein the first human immunoglobulin is selected IgG1, IgG2, and IgG4, and the second human immunoglobulin is selected from IgG2 and IgG4.

3. A binding molecule as claimed in claim 1 or claim 2 wherein 2 amino acids in 1 region of the C_H2 domain are modified to the corresponding amino acids from a second human immunoglobulin heavy chain C_H2 domain.

4. A binding molecule as claimed in any one of the preceding claims wherein at least 2 amino acids in each of the 2 discrete regions of the C_H2 domain are modified to the corresponding amino acids in the corresponding region in a second and third human immunoglobulin heavy chain C_H2 domain respectively.

5. A binding molecule as claimed in any one of the preceding claims wherein the effector domain shares at least

about 90% sequence identity with the first human immunoglobulin heavy chain C_H2 domain.

6. A binding molecule as claimed in any one of the preceding claims comprising a human immunoglobulin heavy chain C_H2 domain having one or more of the following amino acids or deletions at the stated positions in accordance with the EU numbering system:

Posn	Amino acid
233	P
234	V
235	A
236	(No residue) or G
327	G
330	S
331	S

7. A binding molecule as claimed in any one of the preceding claims comprising a human immunoglobulin heavy chain C_H2 domain having one or more of the following blocks of amino acids or deletions at the stated positions in accordance with the EU numbering system: 233P, 234V, 235A and no residue at 236; or 233P, 234V, 235A and 236G; and/or 327G, 330S and 331S.

8. A binding molecule as claimed in any one of claims 5 to 7 wherein the effector domain is selected from G1Δab, G2Δa or G1Δac.

9. A binding molecule as claimed in any one of the preceding claims further comprising modifications to render the molecule substantially null allotypic.

10. A binding molecule as claimed in any one of the preceding claims wherein the effector domain has a reduced affinity for FcγRI, FcγRIIa or FcγRIII and a reduced ability to mediate complement lysis by comparison with the first or second human immunoglobulin heavy chain C_H2 domain.

11. A binding molecule as claimed in claim 10 wherein the effector domain has retained an affinity for FcγRIIb.

12. A binding molecule as claimed in any one of the preceding claims wherein the binding domain derives from a different source to the effector domain.

13. A binding molecule as claimed in any one of the preceding claims wherein the binding domain is selected from the binding site of an antibody; an enzyme; a hormone; a receptor; a cytokine or an antigen; a ligand or an adhesion molecule.

14. A binding molecule as claimed in any one of the preceding claims wherein the binding domain is capable of binding any of: the RhD antigen of red blood cells; an HPA alloantigen of platelets; a neutrophil antigen; a T-cell receptor; integrin; GBM collagen; Der P1; HPA-1a; VAP-1; laminin; lutheran; platelet glycoprotein VI; platelet glycoprotein Ia/IIa.

15. A binding molecule as claimed in claim 14 wherein the binding domain is selected from that of CAMPATH-1 and FOG1; OKT3; B2 (anti-HPA-1a); VAP-1; murine anti-α3 (IV) NC1; YTH12.5 (CD3); 2C7 (anti-Der p I); anti-laminin; anti-lutheran.

16. An isolated nucleic acid comprising a nucleotide sequence encoding the effector domain of the binding molecule as claimed in any one of the preceding claims.

17. A nucleic acid as claimed in claim 16 wherein the nucleotide sequence encodes a binding molecule as claimed in any one of the preceding claims.

18. A nucleic acid as claimed in claim 16 or claim 17 which is a replicable vector.

19. A nucleic acid as claimed in claim 18 wherein the nucleotide sequence is operably linked to a promoter.

20. A host cell comprising or transformed with the vector of claim 19 or claim 20.

21. A process for producing a binding molecule as claimed in any one of claim 1 to 15, the process comprising the step of modifying a nucleotide sequence encoding a first human immunoglobulin heavy chain C_H2 such that 2, 3 or 4 amino acids in at least 1 region of the C_H2 domain corresponds to an amino acid from a second human immunoglobulin heavy chain C_H2 domain,

wherein the region is selected from the 2 discrete regions

numbered residues 233-236, and 327-331 in accordance with the EU numbering system,

and wherein in each case the human immunoglobulin is selected from IgG1, IgG2 and IgG4.

22. A process as claimed in claim 21 wherein 2 amino acids in 1 region of the C_H2 domain are modified to the corresponding amino acids from a second human immunoglobulin heavy chain C_H2 domain.

23. Use of a binding molecule or nucleic acid as claimed in any one of claims 1 to 19 to bind a target molecule with said binding molecule.

24. Use as claimed in claim 23 wherein the target molecule is FcγRIIb, which binding causes inhibition of one or more of: B cell activation; mast cell degranulation; phagocytosis.

25. Use as claimed in claim 24 to prevent, inhibit, or otherwise interfere with the binding of a second binding molecule to the target molecule.

26. Use as claimed in claim 25 wherein the second binding molecule is an antibody.

27. Use as claimed in claim 25 or claim 26 wherein the target molecule is selected from: the RhD antigen of red blood cells; an HPA alloantigen of platelets; a neutrophil antigen; a T-cell receptor; integrin; GBM collagen; Der P1; HPA-1a; VAP-1; laminin; lutheran; platelet glycoprotein VI; platelet glycoprotein Ia/IIa.

28. Use as claimed in any one of claims 24 to 27 for the treatment of a patient for a disorder selected from: Graft-vs-host disease; host-vs-graft disease; organ transplant rejection; bone-marrow transplant rejection; autoimmunity such as vasculitis, autoimmune haemolytic anaemia, autoimmune thrombocytopenia and arthritis; alloimmunity such as foetal/neonatal alloimmune thrombocytopenia; asthma and allergy; chronic or acute inflammatory diseases such as Chrohn's; HDN; Goodpastures, sickle cell anaemia, coronary artery occlusion.

29. Use as claimed any one of claims 23 to 28 wherein the binding molecule is administered to a patient, or optionally

in cases where the patient is an unborn infant, to the mother of the patient.

30. A pharmaceutical preparation comprising a binding molecule as claimed in one of claims 1 to 15, or a nucleic acid as claimed in any one of claims 17 to 19, plus a pharmaceutically acceptable carrier.

31. An oligonucleotide selected from:
MO22BACK: 5' TCT CCA ACA AAG GCC TCC CGT CCT CCA TCG AGA AAA 3'
MO22: 5' TTT TCT CGA TGG AGG ACG GGA GGC CTT TGT TGG AGA 3'
MO7BACK: 5' TCC TCA GCA CCT CCA GTC GCG GGG GGA CCG TCA GTC 3'
MO21: 5' GAC TGA CGG TCC CGC GAC TGG AGG TGC TGA GGA 3'